

WHAT IS CLAIMED IS:

1. A viral vector comprising a nucleic acid encoding a therapeutic polypeptide, wherein said nucleic acid is operably linked to a heterologous destabilizing element, wherein upon introduction of said vector into a target cell, expression of said therapeutic
5 polypeptide encoded by said nucleic acid is enhanced in said target cell relative to the expression of said therapeutic polypeptide in a non-target cell into which said vector has been introduced.
2. The vector of claim 1, wherein said target cell is a tumor cell.
- 10 3. The vector of claim 1, wherein said heterologous destabilizing element is radiation responsive.
4. The vector of claim 1, wherein said heterologous destabilizing element is responsive
15 to inflammatory mediators.
5. The vector of claim 4, wherein said heterologous destabilizing element is the 3' untranslated region of the tumor necrosis factor alpha gene.
- 20 6. The vector of claim 1, wherein said heterologous destabilizing element is stabilized in proliferating cells.
7. The vector of claim 1, wherein said heterologous destabilizing element is responsive to activated RAS and elevated P-MAPK activity.
- 25 8. The vector of claim 7, wherein said heterologous destabilizing element is the 3' untranslated region of the cyclooxygenase 2 gene.
9. The vector of claim 1, wherein said heterologous destabilizing element is responsive
30 to hypoxic conditions.

10. The vector of claim 9, wherein said heterologous destabilizing element is the 3' untranslated region of the vascular permeability factor/vascular endothelial growth factor gene.

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11. The vector of claim 9, wherein said heterologous destabilizing element is the 3' untranslated region of the urokinase plasminogen activator receptor gene.

12. A conditionally replication competent viral vector, said vector comprising an essential gene operably linked to a heterologous destabilizing element, wherein upon introduction of said vector into a target cell, expression of the essential gene product encoded by said essential gene is enhanced in said target cell relative to the expression of the essential gene product in a non-target cell into which said viral vector has been introduced.

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13. The viral vector of claim 12, wherein said target cell is a tumor cell.

14. The viral vector of claim 12, wherein said viral vector is an adenoviral vector.

20 15. The viral vector of claim 14, wherein said essential gene is E1A.

16. The viral vector of claim 12, wherein said viral vector is a vaccinia virus vector.

17. A method of treating a patient having a tumor, said method comprising administering to said patient a conditionally replication competent viral vector, said vector comprising an essential gene operably linked to a heterologous destabilizing element, whereby expression of the essential gene product encoded by said essential gene is enhanced in cells within the tumor relative to expression of the essential gene product in non-tumor cells into which the virus has been introduced.

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18. The method of claim 17, wherein said virus is an adenovirus.

19. The method of claim 18, wherein said essential gene is the E1A gene.

20. The method of claim 17, wherein said virus is a vaccinia virus.

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21. The method of claim 17, wherein said heterologous destabilizing element is radiation responsive, responsive to inflammatory mediators, stabilized in proliferating cells, responsive to activated RAS and elevated P-MAPK activity, or responsive to hypoxic conditions.

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22. A method of treating a patient having a tumor, said method comprising administering to said patient a viral vector, said vector comprising a nucleic acid encoding a therapeutic polypeptide operably linked to a heterologous destabilizing element, whereby expression of said therapeutic polypeptide is enhanced in cells within said tumor relative to expression of said therapeutic polypeptide in non-tumor cells into which said virus has been introduced.

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